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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,912	05/16/2006	Federico Mailland	622-91	5633

23117 7590 02/19/2010

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	PAPER NUMBER
1628	
MAIL DATE	DELIVERY MODE
02/19/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,912	MAILLAND, FEDERICO	
	Examiner	Art Unit	
	JENNIFER M. KIM	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *November 30, 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed November 11, 2009 have been received and entered into the application.

Response to Arguments

Applicant's arguments filed November 30, 2009 have been fully considered but they are not persuasive. With regard to the 35 U.S.C. 112, first paragraph rejection, Applicant argues that the Examples 4 and 5 in the instant specification clearly relate to the prevention of vaginal fungal infections, and do not refer to the treatment of vaginal fungal infections. The disclosed examples have been carefully considered and reviewed. However, they are not persuasive because with regard to example 4, it is clear from the examples that the subject population that underwent a follow up therapy with ascorbic acids described as those forty women **with** exacerbation of recurrent vaginal candidiasis. Therefore, these patients are already suffering from the fungal infection. Accordingly, the example provided by the specification is directed toward the treatment rather than prevention of fungal infections. With regard to example 5, there were 95 patients with the active group and 92 patients with the placebo group were included in the efficacy analysis and the results showed a Candida superinfection in 14 patients (15%) of placebo group and respectively in 9 patients (9%) of active group. It is not clear how the Candida was successfully “prevented” by having 9% of active group

compared with 15% of the placebo group. It is highly speculative that 9% of active group compared with 15% placebo group and the protection factor of ascorbic acid against Candida superinfection showing only 40% would justified the instantly claimed "prevention". Therefore, a method for the **prevention or** treatment of vaginal fungal infections which comprises the administration of a formulation comprising ascorbic acid or a physiologically acceptable salt thereof to a patient in need of such a treatment wherein said formulation is administered after completion of the standard treatment against fungal infections is not considered to be enabled by the instant specification. With regard to 35 U.S.C. 103 rejection, Applicant argues that the present invention is based on the discovery that ascorbic acid creates an unfavorable environment to the germination of fungal spores after a standard treatment against bacterial, fungal or protozoarian injections which is not suggested by Zeng or Hotzel. This is not persuasive because the mechanism of action of ascorbic acid creates an unfavorable environment to the germination of fungal spores by which the active ingredient gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. That is, vitamin C is known to favors the selection and colonization of lactobacillus that is known to inhibit the growth of fungi. It is also known that vitamin C helps to activate the immunodefense system as taught by Hotzel et al. An explanation of why that effect is an unfavorable environmental to the germination of fungal spores does not make unobvious the treatment of the conditions encompassed by the claims.

Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 18-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treatment of vaginal fungal infections", does not reasonably provide enablement for the "**prevention** of vaginal fungal infections". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method for the prevention and treatment of vaginal fungal infections which comprises the administration of a formulation comprising ascorbic acid or a physiologically acceptable salt thereof to a patient in need of such a treatment wherein said formulation is administered after completion of the standard treatment against bacterial, fungal or protozoarian infections. The nature of the invention is extremely complex in that it encompasses the actual **prevention** of fungal infections (i.e. mycoses) such that the subject treated with above compounds does not contract fungal infections.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass **prevention** of fungal infections in humans which has potentially many different causes (i.e. many different group of fungi). Each of which may or may not be addressed by the administration of the claimed compound.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually **prevent** the actual development of fungal infections is minimal. All of the guidance provided by the specification is directed towards **treatment rather than prevention** of fungal infections.

Working Examples: All of the working examples provided by the specification are directed toward the treatment rather than prevention of fungal infections.

State of the Art: While the state of the art is relatively high with regard to treatment of fungal infections (i.e. yeast infection), the state of the art with regard to **prevention** of such disorders is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to **prevent** development of fungal infections.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual **prevention** of fungal infections in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of **prevention** of fungal infections.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for **prevention** of fungal infections. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard **prevention** of fungal infections with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the

system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding prevention of fungal infections with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of fungal infections in a subject by administration of one of the claimed compounds.

Therefore, a method for the prevention and treatment of vaginal fungal infections which comprises the administration of a formulation comprising ascorbic acid or a physiologically acceptable salt thereof to a patient in need of such a treatment wherein said formulation is administered after completion of the standard treatment against bacterial, fungal or protozoarian infections is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 18-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kerr (1999 ISSN 0891-060X) in view of Hotzel et al. (U.S.Patent No. 5,371,107) of record.

Kerr teaches that the normal vaginal flora consist of lactobacilli. Kerr teaches that alteration in vaginal flora is important in the pathogenesis of vaginosis in general and that lactobacilli has been shown to inhibit the growth of fungi and reduction in their numbers allow yeast to proliferate. Kerr teaches that factors thought to favor development of vaginal candidiasis include antibiotic therapy and changes in vaginal pH. (page 138 left-hand column third full paragraph, page 133 left-hand column second full paragraph).

Kerr does not teach the administration of ascorbic acid, the specified fungal infections set forth in claims 24-27 and the administration to patient after completion of antimicrobial agents set forth in claims 20 and 21.

Hotzel et al. teach that a medicinal composition in the form of an ointment or tablet containing about 3% to about 50% by weight of ascorbic acid. (abstract). Hotzel et al. teach that research with the administration of vitamin C to the vagina can normalize the vaginal flora and activates the immune system. (column 1, lines 20-25, column 2, lines 40-50, lines 62-68). Hotzel et al. teaches that local application to vaginal region of vitamin C is completely atoxic and favors the selection and

colonization of important types of normal flora, i.e. lactobacillus. Patients have a very high tolerance for the long term application of vitamin C and a systematic absorption of vitamin C from the vaginal region is desired and additionally leads to an increased vitamin C supply. There are no objections to vitamin C administration during pregnancy. (column 3, lines 60-column 4).

It would have been obvious to one of ordinary skill in the art to employ Hotzel et al's vitamin C (ascorbic acid) composition for the treatment of vaginal fungal infections after the completion of antimicrobial therapy. One would have been motivated to make such a modification in order to achieve a beneficial effect of ascorbic acid having colonizing important types of normal flora (i.e. lactobacillus) which inhibits the effect of the fungi growth results from antibiotic therapy as taught by Kerr. There is a reasonable expectation of successfully treating vaginal fungal infections with vitamin C (ascorbic acid) composition of Hotzel et al. because vitamin C is known to activate the immune system by normalize the vaginal flora that inhibits the fungi growth. With regard to the initiation of ascorbic acid after the completion of the specified antibiotics set forth in claims 20 and 21, such is obvious because it is well known in the art that after a completion of an antibiotic treatment, there is increased chance of the patient having a fungal infection due to the antibiotic treatment destroying a normal flora as taught by Kerr. With regard to the cause of the fungal infections set forth in the claims 24-27 such is obvious because the effectiveness of vitamin C (ascorbic acid) for normalizing and activating the immune system would be retained regardless of the cause. For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the

state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JENNIFER M KIM/
Primary Examiner, Art Unit 1628

Jmk
January 21, 2010